REMARKS

By this action, Claims 6 and 8 have been amended. Claims 18, 19, and 22 have been cancelled. Thus, Claims 2, 6-9, 11, 20-21, and 23-24 are pending.

A. Rejections Under 35 U.S.C 112, first paragraph

Claims 6, 8, and 9 stand rejected under 35 U.S.C. 112, first paragraph, for containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed. Specifically, the Examiner states that the term "molar ratio" in claims 6 and 8 lacks proper support in the specification.

Applicants traverse and direct attention to the experimental results discussed at page 13, paragraph 33, in which it is stated that at "a stoichiometric concentration (corresponding to a neomycin to binding site ratio of 1) neomycin inhibits RT-induced cleavage at the primary site by 80%, achieving total inhibition to binding site ratio of 5 (Fig. 1c). The "stoichiometric" concentration means the same as molar concentration. Support for this assertion is found in Figure 1(c).

Figure 1(c) is a graph with "neomycin/binding site" as the X-axis and "percent cleavage" as the Y-axis. The X-axis is a molar ratio. To this end, claims 6 and 8 have been amended merely to clarify the meaning the RNA-DNA hybrid substrate by adding the words "binding site, which are the same words used on the X axis. As shown in Figure 1(c), at a ratio of 1:1 (the number 1 on the X axis), the percentage cleavage is less than 25%--around the 20% range, which is how the 80% inhibition is calculated. At a ratio of 5:1 (the number 5 on the X-axis), the percentage cleavage is zero, which means that cleavage is 100% inhibited. Thus, the specification, which includes the drawings, describes the where the molar ratio numbers are derived. Applicants respectfully request withdrawal of this rejection.

B. Rejections Under 35 U.S.C. 112, second paragraph

Claims 21 and 24 stand rejected under 35 U.S.C. 112, second paragraph, for being indefinite in that they fail to particularly point out and distinctly claim the subject matter that

the Applicants regard as the invention. Specifically, the Examiner states that the term "A-like" in claims 21 and 24 renders the claims indefinite because this element is not actually disclosed in the specification. Applicants respectfully submit that this rejection is without merit because the term was sufficiently disclosed in the specification. Additionally, the term "a-like" or "a-form" with respect to nucleic acid is a term of art.

Page 4, paragraph 10 of the specification states that in a preferred embodiment, the ligand of the invention (neomycin) "preferentially binds A-form and/or A-like conformations of nucleic acids." This paragraph states that aminoglycosides of the neomycin class are known to preferentially bind A-form rather than B-form nucleic acid structures, and cites two references in support of this assertion: Robinson, H. and Wang, A.H.-J., "Neomycin, spermine and hexaamminecobalt(III) share common structural motifs in converting B- to A-DNA", Nucleic Acids Res 24:676-682, (1996); and Chen, Q., Shafer, R.H., and Kuntz, I.D., "Structure-based discovery of ligands targeted to the RNA double helix", Biochemistry 36:11402-11407 (1997). Page 5, paragraph 11 goes on to state that one of the characteristics of the RNA-DNA substrate of reverse transcriptase RNase H is its adoption of A-like conformation, citing for support Saenger, W., "Principles of Nucleic Acid Structure", 220-241 (Springer-Verlag, New York, 1984).

These statements are essentially repeated on page 11, paragraph 28 of the specification, which states that "one of the structural characteristics of RNase H RNA-DNA hybrid duplexes is that they adopt A-like conformations." The paragraph explains that a preferred embodiment of the invention provides for inhibition of RT RNase H activity by introduction of agents that target A-like conformations of the RNA:DNA hybrid substrate of RNase H. Paragraph 29 also restates the fact that one structural characteristic of RNA-DNA hybrid duplexes is their adoption of A-like conformations, and that aminoglycosides of the neomycin class are known to preferentially bind A-form relative to B-form nucleic structures.

All publications that explain the meaning of A-like conformation are incorporated by reference (See Paragraph 55). The term is not indefinite because its elements are disclosed in the referenced publications. Further, the term "A-like" with respect to nucleic acid conformations is clearly known in the art and is not "unascertainable" as the office action

claims. A definition of "a-form DNA" from an online biomedical dictionary is attached with this response as evidence. Thus, this term is defined both in the specification and is commonly known, as so this rejection should be withdrawn.

C. Rejections under 35 U.S.C. 103

Claims 2, 6-9, 11-12, and 18-24 stand rejected under 35 U.S.C. 103(a) as obvious in light of U.S. Patent No. 5,534,408 ("Green"). Green discloses the use of specific small organic molecules (preferably, 2-DOS aminoglycosides), including neomycin, to inhibit binding of HIV Rev protein to RNA that contains a Rev-responsive element. HIV Rev protein acts posttranscriptionally to facilitate transport of HIV env mRNA's from the nucleus to the cytoplasm. If Rev is unable to bind these RNAs, they do not get transported to the cytoplasm and HIV replication is inhibited. Green does not expressly teach the treatment of HIV infected patients with neomycin, but the Examiner states that this use would have been obvious to one skilled in the art. Solely for the purpose of speeding prosecution, Applicants have cancelled Claims 18, 19, and 22, which referred to treating diseases and HIV. The methods of Green and the present invention clearly operate in distinct manners.

The teachings of Green have little bearing on claims 2, 6-9, 11-12, and 20-21, and 23-24. These claims are specifically drawn to a method of inhibiting the activity of a particular protein, namely the RNase activity of reverse transcriptase. The method of the present invention occurs much earlier in the viral life cycle than the interaction studied by Green. The ability of neomycin to inhibit reverse transcriptase activity was previously unknown in the art. Based on the teachings of Green, it certainly would not have been obvious to one skilled in the art that neomycin was capable of inhibiting reverse transcriptase activity. Green makes no mention of reverse transcriptase or of its duplex DNA:RNA substrate. By stating that the mechanism of neomycin-mediated HIV replication arises from disruption of the Rev-RNA interaction, Green is actually teaching away from the use of neomycin to inhibit reverse transcriptase. Green would be assuming that neomycin would not act in the

viral replication life cycle until it inhibited the binding of the Rev protein, which teaches away from the present invention where neomycin acts on an earlier replication step.

The Action asserts that the "instant claims are directed to effecting a biochemical pathway with an old and well known compound. It is well settled that the mode of elucidation does not impart patentable moment to otherwise old and obvious subject matter (citing In re Swinehart)." The flaw in this reasoning is that, in the present case, the known compound (neomycin) is used to effect a different chemical pathway than the one disclosed in Green. The use of a compound, which has been patented for use in a first method, in a second, separate method, operating by a separate mechanism is patentable.

Also, citation of the In re Swinehart case ((169 USPQ 226 at 229 (CCPA 1971)) is inapposite. In re Swinehart involved a "composition of matter" (compound) being claimed functionally, which had a newly discovered, inherent property. In contrast, the present application claims a new **method of using** a compound, **not the compound itself**. Thus, Green does not make the pending claims obvious and the rejection should be withdrawn.

CONCLUSION

In view of the above, each of the newly presented claims in this application is believed to be in immediate condition for allowance. Accordingly, applicant respectfully requests that the Examiner withdraw the outstanding rejections and pass this application to issue.

The Commissioner is authorized to charge any fees required by the filing of these papers, and to credit any overpayment to Perkins Coie's Deposit Account No. **50-2586**. If anything can be done to further this application, please contact the undersigned at 310-788-9900.

Respectfully submitted,

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a-form DNA

<molecular biology> One of several forms that can be assumed by a double helix. A-DNA is stable in dehydrated conditions.

This form is less common than the dominant form found under physiological conditions -- beta-DNA. This form is also assumed by DNA-RNA hybrid helices and by regions of double-stranded RNA. It is a right-handed helix and is a more compact form than beta-DNA.

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Previ us: aflatoxin B1 reductase, aflatoxin G2a reductase, aflatoxin m1, AFLP, AFO
Next: AFORMED phenomenon, AFP, africa, eastern, african

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